

### **REMARKS/ARGUMENTS**

In the communication mailed January 7, 2005, the Examiner has rejected claims 1 through 5, 7 through 9, 12 and 13 under 35 U.S.C. 112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner asserts that in claims 1 through 5, "A" is defined as "imino," which suggests "-N=C-." However, in compound names and structures, it appears that "A" can be "amino" or "-NH." Additionally, the Examiner states that claim 5 lacks antecedent basis in that E maybe "*N*-methyl-*N*-(tetrahydrofuran-3-yl)amino" and "*N*-methyl-*N*-(tetrahydropyran-4-yl) amino," neither of which is recited in the definition of E in claim 1.

Additionally, the Examiner has rejected Claims 1 through 5, through 9, 12 and 13 under the judicially created doctrine of obviousness-type double patenting over claims 1 and 6 through 9 of U.S. Patent 6,627,634 (the '634 patent.) Finally, claims 1 through 6 are provisionally rejected under the judicially created doctrine of obvious-type double patenting as being unpatentable over claims 1 through 6 of co-pending application U.S.S.N. 10/023,099 the ('099 application).

Reconsideration of the rejection in view of the instant amendment and the following remarks is respectfully requested.

Upon entry of the instant amendment prior claims 1 through 9, 12 and 13 will be cancelled. In their place are newly added claims 14 through 24. The correspondence below indicates how newly added claims 14 through 24 correspond to the rejected claims:

#### **Cancelled Claim**

#### **New Claim**

1	14	(All prior amendments to 1 incorporated)
2	15	(all prior amendments to 2 incorporated)
3	16	(all prior amendments to 3 incorporated)
4	17	(all prior amendments to 4 incorporated)
5	18	(all prior amendments to 5 incorporated, plus new amendment to definition of E)

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|----|----|--|
| 6  | 19 | (amended to depend from claim 14)  |
| 7  | 20 | (amended to depend from claims 14 through 19)  |
| 8  | 21 | (all prior amendments to 8 incorporated and amended to depend from claims 14 through 19) |
| 9  | 22 | (all prior amendments to 9 incorporated and amended to depend from claims 14 through 19) |
| 10 |    | Previously cancelled   |
| 11 |    | Previously cancelled   |

Concerning the use of the term imino, the IUPAC Compendium of Chemical Terminology (2<sup>nd</sup> Ed. 1997) indicates that “imino” can have the meanings given to it by the subject application, that is, both “-NH-“ and “-N=C-.”(copy enclosed) It is respectfully submitted that one skilled in the art could determine the meaning of “imino” from the context in which the term occurs. That is, with the definition of the neighboring groups, it is possible to know whether it will be “-N=” or “-NH<sub>2</sub>” to one skilled in the art.

Regarding the definition of E in claim 5, the Examiner is correct. Accordingly, claim 5 is cancelled, and replaced with new claim 18.

Concerning the double-patenting rejection over the ‘634 patent, the Examiner refers to the definition of C in the ‘634 patent and treats such as equivalent to the definition of E in the subject application where E is C<sub>1-4</sub>-alkylamino or di-(C<sub>1-4</sub>-alkyl) amino. This is not a valid comparison since according to the ‘634 patent the C<sub>2-4</sub> alkyl (C being a C<sub>2-4</sub>- alkyl-NR<sub>4</sub>-group) must be substituted by a group containing R<sub>6</sub> or by a 2-oxomorpholino group. (see the ‘634 patent, column 5, lines 31-36) R<sub>6</sub> is a 2-oxotetrahydrofuran-4-yl, 2-oxotetrahydropyrany-4-yl, or 2-oxotetrahydroprany-5-yl group optionally substituted by one or two C<sub>1-2</sub>-alkyl groups (see the ‘634 patent, column 3, lines 33 to 38). R<sub>6</sub> as a substituent is defined in the ‘634 patent to cover only lactone groups (cyclic esters) since the oxotetrahydrofuran- and tetrahydropyran rings contain a carbonyl group within the ring attached to the ring oxygen atom, resulting in the structural element -C(O)-O-. The same applies to the oxo-morpholino group.

Thus, if one carefully reads the definition of C in the '634 patent, starting in column 2, line 24, it will become clear that the presence of a lactone substructural element is mandatory, either defined via subgroups D, E, R5 or R6, or via the presence of 2-oxomorpholino.

The definition of E in the subject application does not include any lactones. The difference is significant in terms of the properties of the claimed compounds. The lactones disclosed in the '634 patent are hydrolyzed easily in plasma, and are therefore suitable for topical or inhalative administration. They are active on the skin or in the lungs, but inactivated rather quickly when orally absorbed, thus avoiding systemical side effects. In contrast, the compounds of the subject application are stable in plasma, and so are suitable for oral or parenteral administration.

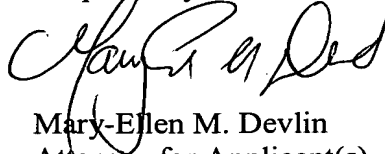
This means that the compounds of the subject application are suitable for co-administration with other cancer agents, which are generally dosed either orally or via parenteral administration.

Concerning the provisional double-patenting rejection over the '099 application, such rejection will be addressed when there is allowance of claims in the '099 application.

Application No. 10/016,280  
Amdt dated July 7, 2005  
Reply to Office action of January 7, 2005

In view of the foregoing, it is respectfully submitted that the subject application is in condition for allowance and such favorable action at an early date is earnestly solicited.

Respectfully submitted,



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